REVIEW ARTICLE

Fish and shellfish allergy in children: Review of a persistent food allergy

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Abstract

The increased consumption of fish and shellfish has resulted in more frequent reports of adverse reactions to seafood, emphasizing the need for more specific diagnosis and treatment of this condition and exploring reasons for the persistence of this allergy. This review discusses interesting and new findings in the area of fish and shellfish allergy. New allergens and important potential cross-reacting allergens have been identified within the fish family and between shellfish, arachnids, and insects. The diagnostic approach may require prick to-prick tests using crude extracts of both raw and cooked forms of seafood for screening seafood sensitization before a food challenge or where food challenge is not feasible. Allergen-specific immunotherapy can be important; mutated less allergenic seafood proteins have been developed for this purpose. The persistence of allergy because of seafood proteins' resistance after rigorous treatment like cooking and extreme pH is well documented. Additionally, IgE antibodies from individuals with persistent allergy may be directed against different epitopes than those in patients with transient allergy. For a topic as important as this one, new areas of technological developments will likely have a significant impact, to provide more accurate methods of diagnosing useful information to patients about the likely course of their seafood allergy over the course of their childhood and beyond.

Increased consumption of seafood because of its high nutritive value and the promotion of a healthy diet may also have led to the more frequent reporting of adverse reactions, including immunologic-mediated reactions. In countries where the consumption is high, such as in Scandinavia, Portugal, and Spain, it is one of the most common food allergens (1).

Unfortunately, fish and shellfish allergies can be important causes of severe acute hypersensitivity reactions, including fatal anaphylaxis (2). Furthermore, although children can develop tolerance to most common food allergens, the potential for persistence of seafood allergy should be considered when counseling families regarding its expected clinical course. The purpose of this review is to summarize the evidence regarding fish and seafood allergy, identify knowledge gaps, and discuss directions for future management and treatment.

Edible seafood can be categorized into three phyla: Mollusca, Arthropoda, and Chordata, each subdivided into multiple classes and species (3) (Table 1). The two invertebrate phyla, molluscs and crustaceans, are generally referred to as 'shellfish' in the context of seafood consumption. The phylum Chordata includes finned fish, with the major component consisting of the class Osteichthyes (salmon, tuna, cod, hake) (3). The group of fish can be subdivided into the bony fish, to which most edible species belong, and the cartilaginous fish. Because of the wide diversity of species, both patients with fish or shellfish allergy and their treating physicians may fail to identify the offending species, a problem compounded by the many different common names used to describe fish and shellfish.

Original research studies published in English between 1985 and 2011 were selected (PubMed and Scopus). Computer

Table 1 Classification of seafood species

Phylum	Class	Species
Mollusca	Gastropoda	Abalone (Perlemoen), Snails, Alikreukel
	Bivalvia	Mussels, Oysters, Clams, Scallops
Arthropoda	Cephalopods	Squids (Calamari), Octopus, Scallop
	Crustaceans	Lobsters, Shrimp, Prawn, Crayfish (freshwater), Crab Rock Lobster (Kreef)
Chordata (fish)	Chrondrichthyes (cartilaginious fish)	Sharks, Rays, Skates
	- Lamniformes	
	Osteichthyes (bony fish)	Cod, Haddock, Hake
	- Cadiformes	
	- Salmoniformes	Trout, Salmon, Pike
	- Perciformes	Snapper, Mackerel, Tuna, Bonito, Grouper
	- Pleurenectiformes	Sole, Flounder, Halibut, Plaice

searches used combinations of key words relating to 'allergy' and 'fish or seafood'. In addition, the reference lists of the retrieved articles helped in the search for other relevant articles, which were not found during the searching initial procedure. Thus, 32 studies were selected and discussed here (15 cross-sectional, 9 case–control, and 8 population-based studies). The potential factors that may bias the findings of this review are restriction articles in English, together with database and citation bias.

Epidemiology

It is generally considered that fish and crustaceans are among the four food groups most commonly provoking anaphylactic reactions. The prevalence of fish and seafood allergy is usually higher in communities where fish or shellfish constitute a large proportion of the diet, such as China, Japan, and USA, which are the three largest global consumers of fish (4). Regarding fish, cod, tuna, salmon, trout, and plaice have been involved in food-allergic reactions in the United States, United Kingdom, and Europe. Few well-known species are often eaten in other countries (5). The prevalence of fish allergy is low in children (≤0.2%), although the prevalence of shellfish allergy remains low, but higher than the fish allergy (≤0.5%) (5).

Despite the ubiquity of fish and seafood in the diet, no studies have specifically addressed the prevalence, which is predominantly based on self-reported than physician-diagnosed and/or convincing reactions. Allergy to some types of seafood was reported for 0.6% of US children younger than 18 yr of age, and fish allergy accounts for an estimated 0.1% of food allergies in US children (6). In Norway, adverse food reactions were reported by parents in 30% of their children, nearly 3% attributable to fish by age of 2 yr (7). A study from Singapore of 227 children with food hypersensitivity confirmed that crustacean and fish are significant sensitizers in about 40% and 13% of children, respectively. Interestingly, the first intake of seafood seems to be very early in life in Asian diet, with an average age of as low as 7 months (8).

Allergens in fish and shellfish

Many allergens have been analyzed in fish and shellfish (Table 2) (9–26). Codfish and shrimp have been the models used to study allergy to fish and shellfish, respectively.

Codfish allergy is the best studied; Gad c 1, the major cod allergen, is a parvalbumin believed to be similar in structure to those present in many fish species (9). Parvalbumin is a calcium-binding sarcoplasmic protein with a molecular mass of about 12 kDa, resistant to heat, chemical denaturation, and proteolytic enzymes (9). Parvalbumins are present in high amounts in white muscle of lower vertebrates and in lower amounts (27) in fast twitch muscles of higher vertebrates (28). Bony fish have fast-twitching white muscle for continuous swimming. Active fish, such as tuna, skipjack, and swordfish, have a higher proportion of dark muscle than bottom-dwelling fish, such as cod, flounder, or whiff (29). Dark muscle contains lower levels of parvalbumins, thus these fish species are expected to be of lower allergenicity (29, 30).

In shellfish, such as crustacean and molluscs, the major allergen responsible for ingestion-related allergic reactions is the muscle protein, tropomyosin. In addition to tropomyosin, other allergens have been identified and characterized in crustaceans such as the 40-kDa arginine kinase, which might be a new class of invertebrate pan-allergens (31).

Cross-reactivity with other allergen sources

Extensive cross-reactivity between different species of seafood has been demonstrated (Table 3).

Cross-reactivity within the fish group

Parvalbumins share various degrees of amino acid homologies ranging from 60% to 80%, which probably explains variable degrees of clinical cross-reactivity in patients with fish-allergy. However, patients allergic to codfish may often ingest some other species without risk of allergic symptoms. It is of note that seafood species, that is, crustacean and mollusc allergens, do not cross-react with fish allergens, and no cross-reactivity between known allergens or homologous proteins has currently between demonstrated (1). However, recent epidemiological data report that 21–43% of fish-allergic individuals are also allergic to shellfish (5, 32). Certainly, tropomyosins are not an allergen in non-crustacean fish. Hence, this cross-reactivity could be attributed to the increased atopic predisposition (asthma, allergic rhinitis, eczema) of the seafood-allergic children.

Even so, it is estimated that 50% of individuals allergic to some type of fish are at risk for reacting to a second species, those allergic to some type of shellfish carry a risk of 75%, because of greater similarity among tropomyosins than parvalbumins (33).

Table 2 Summary of seafood allergens identified

Source of allergen	Nomenclature	Identity	Reference
Fish			
Gadus callarias (Baltic cod)	Gad c 1	Parvalbumin	9
Gadus morhua (Atlantic cod)	Gad m 1	Parvalbumin	10
Salmo salar (Atlantic salmon)	Sal s 1	Parvalbumin	11
Scomber japonicus (mackerel)	Sco j 1	Parvalbumin	12
Scomber australausicus (mackerel)	Sco a 1	Parvalbumin	12
Scomber scombrus (mackerel)	Sco s 1	Parvalbumin	12
Cyprinus carpio (common carp)	Cyp c 1.01/1.02	Parvalbumin	13
Crustacea			
Metapenaeus ensis (greasy backed shrimp)	Met e 1	Tropomyosin	14
Penaeus aztecus (Northern brown shrimp)	Pen a 1	Tropomyosin	15
Penaeus indicus (Indian white shrimp)	Pen i 1	Tropomyosin	16
Penaeus monodon (giant tiger shrimp)	Pen m 2	Arginine kinase	17
Homarus americanus (American lobster)	Hom a 1	Tropomyosin	18
Panulirus stimpsoni (Chinese spiny lobster)	Pan s 1	Tropomyosin	18
Charybdis feriatus (red crab)	Cha f 1	Tropomyosin	19
Mollusca			
Haliotis midae (abalone)	Hal m 1	Tropomyosin	20
Haliotis diversicolor (abalone)	Hal d 1	Tropomyosin	21
Turbo cornutus (turban shell)	Tur c 1	Tropomyosin	22
Helix aspersa (brown garden snail)	Hel as1	Tropomyosin	23
Perna viridis (mussel)	Per v 1	Tropomyosin	24
Chlamys nobilis (scallop)	Chl n 1	Tropomyosin	24
Crassostrea gigas (Pacific oyster)	Cra g 1 Cra g 2	Tropomyosin	25
Todarodes pacificus (squid)	Tod p 1	Tropomyosin	26

Table 3 Overview of potential cross-reacting allergens

Allergen identified	Species implicated	Molecular weight (KD)
Parvalbumins	Baltic cod (*Gadus callarias*) Atlantic cod (*Gadus morhua*) Atlantic salmon (*Salmo salar*) Edible frog (*Rana esculenta*)	11.5–12.3
Tropomyosins	Greasyback shrimp (*Metapenaeus ensis*) Brown shrimp (*Penaeus aztecus*) Shrimp (*Penaeus indicus*) Crab (*Charybdis feriatus*) Lobster (*Homarus americanus*) Squid (*Todarodes pacificus*) Snail (*Helix aspersa*) Abalone (*Haliotis midae*) Mites (*Blomia tropicalis*) European house dust mite (*Dermatophagoides pteronyssinus*) American house dust mite (*Dermatophagoides farinae*) American cockroach (*Periplaneta americana*) Silverfish (*Lepisma saccharina*)	32.8–49
Arginine kinase	Black tiger shrimp (*Penaeus monodon*)	40

Cross-reactivity within the shellfish group

Tropomyosin is the major allergen for cross-reactions in different species of the shellfish group (Table 3). Crespos et al. (34) in Spain showed that nine of ten children with sensitization to molluscs reacted by skin prick testing (SPT) and serum-specific IgE to crustaceans. Molecular comparison of tropomyosin from many different crustacean species reveals very high homologies of up to 98%, whereas the amino acid sequence identity of shrimp tropomyosin with mussels and abalone is lower with 57% and 61%, respectively. Hence, it is prudent for all the patients with shellfish-allergy to avoid all shellfish in the absence of evidence of tolerance.

Between shellfish and other invertebrates

Patients with seafood allergy are frequently reported to have allergic reactions to mites and insects. This cross-reactivity is probably due to the high amino acid homology of these invertebrate tropomyosins. In an interesting study (35), a population of orthodox Jews with perennial allergic rhinitis and dust mite/cockroach hypersensitivity, who are prohibited by religious dietary laws from eating shellfish, were found to be SPT positive to shrimp. This sensitization to tropomyosin is probably due to non-crustacean source, such as house dust mites (HDM), cockroaches, or both, via inhalation.

Clinically relevant cross-reactivity between crustacean and HDM allergens has been described, and the term 'mite–crustacean–mollusc syndrome' is sometimes used (36). The primary sensitization is believed mostly to be 'respiratory' allergy to dust mites, which in some individuals may cause food-allergic reactions to shellfish, crustaceans, or molluscs. This view is supported by recent observations during immunotherapy to HDM, in which some patients develop clinical sensitization to shellfish tropomyosin, which did not exist before therapy (37).

Reactions not directly because of seafood

Adverse reactions to purported to be because of seafood may in fact result from responses because of food contamination, newly formed toxic products, or preservatives (Table 4) (38).

These adverse reactions can be triggered by a range of substances including Anisakis simplex, scombroid fish poisoning, ciguatera, and paralytic shellfish (Table 4). The most common reactions are because of Anisakis simplex, which is a worldwide-distributed nematode fish parasite with a life cycle involving fish or marine animals that may infect humans and cause severe allergic reactions (39). The eight allergens from this parasite currently characterized include tropomyosin, which cross-reacts with shellfish allergens, as well as paramyosin and different protease inhibitors (40).

Cooking at temperatures for at least 20 min above 60°C or storage in industrial freezers is required to kill the parasite. The clinical signs of anisakiasis depend on where in the digestive tract the larva is deposited and may develop as a result of an inflammatory response (41). The larvae of Anisakis simplex can also cause an immediate allergic reaction, resulting in systemic signs ranging from urticaria or angioedema to anaphylactic shock (42).

Additionally, a range of adverse reactions can be induced after exposure to sulfites, a preservative, which can be added to shellfish to stop them discoloring. Clinical manifestations of sulfite sensitivity range from dermatitis, urticaria, flushing, hypotension, abdominal pain, and diarrhea to life-threatening anaphylactic and asthmatic reactions (43).

Diagnosis

History

A medical history continues to be the mainstay of the diagnostic process. Unfortunately, the patient is not always able to identify the offending food, because of various factors.

Diagnostic tests and methods

Skin prick testing with the food in question provides a rapid, relatively safe, and inexpensive method for screening patients with a history suggestive of IgE-mediated fish and/or shellfish hypersensitivity. SPT with commercial food extracts is considered to be sensitive, but not specific. The negative predictive value (NPV) is high, although the positive predictive value is rarely higher than 50% (44).

A study from Bangkok, Thailand (45), showed that commercial shrimp extract had the lowest sensitivity and NPV. Besides that, the commercial shrimp extract is usually made from a different species of fish. Therefore, testing of the appropriate species using a crude extract or a prick-to-prick test is very important. In the cases of shrimp allergy, the NPV of 30% from commercial SPT is unacceptable because

Table 4 Summary of common toxic syndromes associated with naturally occurring toxins in seafood (38)

Type of poisoning	Type of toxins	Source	Symptom onset	Clinical syndrome
Scombroid	Histamine	Tuna, mahi-mahi, bonita, marlin, bluefish, wahoo, mackerel, and salmon	Minutes to 4 h	Severe headache, dizziness, nausea, vomiting, flushed skin, urticaria, and wheezing
Ciguatera	Ciguatoxins	Coral reef fish: amberjack, snappers, grouper, goat fish, barracuda, sea bass, surgeon fish, ulua, and papio	30 min to 4 h	Abdominal pain, diarrhea, vomiting, paresthesias, cold-to-hot sensory reversal, weakness, and myalgias
Puffer fish poisoning	Tetradotoxin	Ocean sunfishes, porcupine fishes, and fugu	10–45 min	Paresthesias, headache, vomiting, diaphoresis, and respiratory paralysis
Paralytic shellfish	Saxitoxins	Mussels, clams and oysters	5–30 min	Vomiting, diarrhea, facial paresthesias, and respiratory
Neurotoxin shellfish	Brevetoxins	Mussels and clams	30 min to 3 h	Diarrhea, vomiting, abdominal pain, myalgias, paresthesias, and ataxia
Amnesic shellfish	Domoic Acid	Mussels, clams, crabs, and anchovies	15 min to 38 h	Vomiting, diarrhea, headache, myoclonus, loss of short-term memory, seizures, coma, and hemiparesis
Diarrhetic shellfish	Okadaic acid, Dinophysistoxins, Pectenotoxins, Yessotoxin	Mussels, clams, and scallops	30 min to 6 h	Diarrhea, nausea, vomiting, and abdominal pain

a significant number of sensitive patients will be missed. Although SPT described as being problematic, another study convincingly demonstrated the high predictive probabilities using mean wheal diameters to determine positive food challenges with shrimp (45). SPT is also successfully correlated with positive food challenge when using cooked instead of raw extracts of shrimps and lobster for skin testing (46). The raw shrimp may be less allergenic than cooked shrimp, and the lyophilization of raw shrimp may denature some of the allergens, or the cooking process may alter the protein structure or epitope presentation (46). Additionally, a number of reports suggest that mollusc allergenicity may be increased by heating (20, 47, 48). Given the data (6, 32) on cross-reactivity among fish species and between fish and shellfish, we suggest that patients with fish-allergy should be skin tested to cod fish, as a pan-allergen, (unless clinical reactivity to a specific fish has been shown) and to shellfish as well.

Furthermore, altered fish allergenicity as a result of canning process was demonstrated. In particular, striking loss of definable protein fractions in the canned fish extract when compared with raw and cooked fish extracts and immunoblot analyses demonstrated minimal IgE-specific binding to the canned fish extracts (49). In a recent descriptive study, it was shown that more than 20% of children allergic to salmon or tuna were able to tolerate the fish in a canned form, and this was associated with a reduction in SPT size in most, implying that consumption of canned fish may have resulted in the induction of tolerance in these patients (32).

In vitro diagnostic methods include quantification of specific IgE antibodies using assays such as the ImmunoCAP (Pharmacia, Upsala, Sweden). For fish (cod) allergy, a diagnostic level of IgE that can predict clinical reactivity in a US population with >95% certainty was identified as 20 KU_A/l (50), although diagnostic decision points for specific serum IgE to other species of fish or shellfish are still needed. Diagnostic decision points for serum-specific IgE to shellfish are still needed. However, the problem of serological and clinical cross-reactivity between different fish and shellfish species has not yet been solved.

Food challenge

The gold standard for diagnosing food allergy is still the Double Blind Placebo Controlled Food Challenge (DBPCFC). DBPCFC is the method of choice when day-to-day variations play a major role (as in children with atopic eczema [AE]) or if there are subjective symptoms (e.g., abdominal discomfort, burning of the tongue, palpitations) or isolated digestive late reactions (51, 52). Fig. 1 provides an algorithm for proceeding from the suspicion of seafood-related symptoms to the final decision to recommend a specific elimination diet. However, various decision trees to approach food challenges, including patients with seafood-allergy, have been proposed (51). Patients with a clear-cut case history of anaphylaxis to seafood should not be challenged (52). It is advisable to begin with a starting dose below the expected threshold dose, because this will enable determination of the actual sensitivity in the patient (low

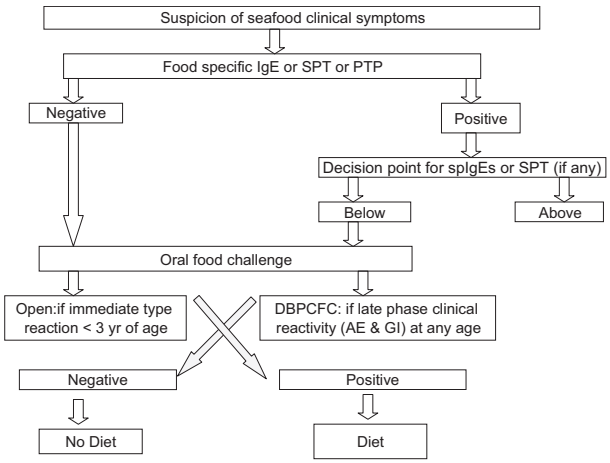

Figure 1 Algorithm for the diagnostic work up of suspected seafood allergy. DBPCFC, double-blind, placebo-controlled food challenges; SPT, skin prick test; PTP, prick to prick; spIgEs, specific IgEs; AE, atopic eczema; GI, gastrointestinal symptoms.

adverse effect level and no observed adverse effect level). Proposed starting dose for fish and shrimp is 5 mg (the actual starting dose must always be considered in the actual patient) (52). Children younger than 3 yr of age will rarely report subjective symptoms. Therefore, these children may undergo open food challenges (OFCs) when AE does not play a role. A single-blind or an OFC may be considered diagnostic under certain circumstances: if either of these challenges elicits no symptoms (i.e., the challenge is negative), then seafood allergy can be ruled out; but when either challenge elicits objective symptoms (i.e., the challenge is positive) and those objective symptoms correlate with medical history and are supported by laboratory tests, then a diagnosis of food allergy is supported (53).

Hence, in everyday practice, the clinical history and the measurement of specific IgEs may help the clinician to differentiate tolerance from allergy, taking into consideration the young age of the children and the issues performing DBPCFC.

Management

The only proven therapy for fish and shellfish hypersensitivity is strict avoidance, which is not always possible. As a result, new approaches to the treatment of food allergy are being investigated and developed. Immunotherapy for food allergy was first described in 1930 (54). In this study, the first successful case of rush immunotherapy for a patient with fish allergy and poorly controlled asthma was reported. In another study, it was described that a young girl with a standard rush immunotherapy protocol with codfish was successfully desensitized (55).

Many alternative approaches, including mutated less allergenic recombinant food proteins, have been developed. Mutant tropomyosin from crustaceans was produced with reduced allergenic potency as demonstrated by rat basophil

mediator release assays, and reduced activation was much more pronounced in the murine model (56). Conformational epitopes are most probably relevant for IgE binding for the major fish allergen, parvalbumin (57). These antibody epitopes seem to be dependent on the functional reactivity of the binding sites for Ca^{2+} and Mg^{2+}. Conformational changes in these helix-loop-helix metal-binding domains by side-directed mutagenesis can result in hypoallergenic parvalbumin, as has been demonstrated for carp (58). Although still immunogenic as demonstrated by IgG response in mice, the reactivity measured by SPT in patients is markedly reduced *in vivo*. This novel hypoallergenic protein is an important basis for safer novel forms of vaccination against fish allergy, but at present, these options require further investigation before they are accepted into clinical practice.

Consequently, dietary avoidance is essential for the management of seafood allergy. We suggest that individuals allergic only to fish or to shellfish are advised to avoid all fish and shellfish species (unless clinical tolerance has been proven to a specific species by challenge). Additionally, performing an OFC to canned fish is a useful strategy for allowing the canned fish to be introduced to the diet of children with fish-allergic when negative. Hence, it can result in a significant improvement to the family's quality of life, particularly as canned fish is widely consumed in Europe.

Nevertheless, it is important not to introduce unjustified restricted diets, particularly as there is an increasing demand to include fish-derived omega-3 fatty acids in the diet because of their possible benefit effects in atopic disease and on health in general (59, 60). Furthermore, in intervention studies, early fish oil supplementation (during pregnancy, lactation, infancy, and childhood) has been shown to lead to immunologic changes, which have a persistent protective effect against allergic diseases (61, 62) and asthma (63).

Prognosis – natural course of fish allergy

In contrast to cow's milk and egg, allergies to fish are usually not outgrown (53). Fish allergy is persistent as around 80% of patients are still allergic even 10 yr after the initial diagnosis.

According to a recent study (64), important differences were seen in the patterns of IgE epitope recognition by children and adults. Compared with adults, children with shrimp allergy on average recognized more shrimp proteins and individual peptides than adults. In addition, the intensity of IgE binding was also greater in children. This has potential implications in the clinical setting. Because shellfish allergy has traditionally been seen as a persistent allergy, once patients are given a diagnosis of shellfish allergy, they typically avoid all shellfish for life. Although we have no doubt that some adults will continue to react to shrimp over time, it is possible that clinical reactivity might decrease as well, given that epitope recognition appears to be less in older subjects. Subjects given diagnoses of shellfish allergy in the past who have decreased allergenic epitope recognition might benefit from an oral shrimp challenge to determine whether they have become tolerant over time.

In a follow-up study, we demonstrated that 65.5% of fish-sensitized children maintained their sensitisation and were at increased risk for wheezing illness and hyperactive airways in school age compared with their non-allergic peers (65). These results are in agreement with another study (66), reporting that allergies to egg, milk, peanut, and fish may serve as early markers for persistent asthma symptoms and increased asthma morbidity, even as children outgrow their food allergies.

Why is this food allergy persistent?

Clinical sensitivity to a certain food often changes over time. Although actual studies are missing, it has been appreciated that allergy to fish and shellfish are usually not outgrown (53). Some results suggest that IgE antibodies from individuals with persistent allergy may be directed against different epitopes than those in patients with transient allergy (67). In addition, it has been shown that egg- and milk-allergic patients with IgE antibodies directed at specific linear epitopes tend to have persistent allergy, whereas those with IgE antibodies primarily to conformational epitopes tend to develop clinical tolerance (68).

Codfish contains one of the most heat-stable major allergens (parvalbumin-Gad c 1), which not only can withstand cooking but also becomes airborne with steam without denaturation. It is also resistant to chemical detergents and is minimally affected by various cooking methods (69). Furthermore, storage has been found to increase its relative capacity for IgE binding, shown by formation of additional bands both in SDS-PAGE and immunoblotting (70). Additionally, in a recent study, it was illustrated that cooked fish extract is more allergenic than raw extract and is capable of eliciting parvalbumin-specific antibody responses (71). The allergenicity is apparently partly conserved even after elaborate food-processing techniques because IgE from patients with fish-allergy still bound to fish proteins after they had been boiled, fried, or canned (72).

Concluding remarks

For a topic as important as this one, the available data are still limited and to some degree confusing.

Extensive cross-reactivity between different species of fish and among molluscs and crustaceans has been demonstrated. Although general opinion and teaching in the allergy/immunology community appears to be that no significant cross-reactivity occurs between crustacean and fish allergy, recent evidence would suggest the opposite. However, a clinically relevant cross-reactivity between shellfish and mites/insects exists, implying the possibility of severe hypersensitivity reactions. Future studies on clinical reactivity will improve diagnosis and management of this life-long allergy. The development of hypoallergenic protein is an important basis for safer novel forms of vaccination against fish allergy, but at present, these options require further investigation before they are accepted into clinical practice.

Additionally, we need to emphasize that SPT using crude extracts or prick to-prick testing with cooked forms of seafood, because of lack of availability and lower NPVs of commercial extracts, are useful and important tools for screening seafood sensitization before a food challenge or where food challenge is not feasible.

Although actual studies are limited, it is now appreciated that allergies to seafood usually persist over time. New areas of technological developments are likely to have a significant impact in providing useful information to patients and their families about the likely course of their seafood allergy over the course of their childhood and beyond, supporting the arguments that IgE antibodies form individuals with persistent allergy may be directed against different epitopes than those in patients with transient allergy. It is hoped that, additional studies will help to clarify further some of these issues, including better laboratory markers of persistent vs. transient food allergy.

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